EXHIBIT 8

1: Haemostasis. 1984;14(4):354-60. Links

The effects of high doses of aspirin and related benzoic acid derivatives on arterial thrombosis in male rats.

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The antithrombotic effects of four compounds structurally related to aspirin (acetylsalicylic acid, ASA) were examined in a rat model of arterial thrombosis and compared to ASA. ASA had antithrombotic activity, but only at high doses (200 mg/kg), when carotid artery thrombosis was induced 15 min after intravenous drug administration. Lower doses were associated with augmented thrombus formation in some animals. 2-Propionyloxybenzoic acid, which has in vitro activities similar to ASA, caused similar in vivo effects, but was antithrombotic at 100 mg/kg. 3-Propionyloxybenzoic acid, which augments platelet function in vitro, and 3-methylphthalide, which inhibits biphasic adenosine diphosphate-induced platelet aggregation, had no statistically significant effects. 2-Acetoxybenzoic acid, which is a weak platelet aggregation and prostaglandin biosynthesis inhibitor, had antithrombotic activity at 100 and 200 mg/kg and was not associated with augmented thrombosis at lower doses as found with ASA. The pattern of antithrombotic activity of this series of compounds does not reflect in vitro effects on prostaglandin biosynthesis and indicates alternative mechanisms of antithrombotic activity.

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